



Administration of Intravenous Immunoglobulin to a Patient with Hypogammaglobulinemia and Anti-IgA Antibodies

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Question:

I understand that anti-IgA antibodies are quite rare in patients with IgA deficiency, but, when starting intravenous immunoglobulin (IVIG) in patients with common variable immune deficiency and with very low serum IgA levels, is the product with the lowest IgA concentration, the only choice or could one choose a product with a low IgA concentration ($<25 \mu\text{g/mL}$)? I know that subcutaneous immunoglobulin (SCIG) would be a safer choice yet, but the patient prefers intravenous administration. Thanks for your thoughts.

Response:

Thank you very much for your inquiry. The role of anti-IgA antibodies in causing adverse reactions from gammaglobulin infusion in patients who are IgA deficient remains controversial. Class-specific anti-IgA antibodies are actually present in approximately a third of patients with IgA deficiency. However, anaphylaxis from IVIG is very rare, which illustrates that the relationship between anti-IgA antibodies and anaphylaxis is not straightforward.

At our center at Boston Children's Hospital, over a period of 15 years, only one case of anaphylaxis was noted in a patient with IgA deficiency and with detectable anti-IgA antibodies and who received IVIG for several years before having an anaphylactic reaction. The patient reacted to an IVIG product that contained $<10 \mu\text{g/mL}$ IgA and later tolerated SCIG with no problem. At the time of initiation of SCIG, the patient had very high class-specific anti-IgA titers. These were not checked at the time of her reaction to IVIG, which occurred 7 years before SCIG initiation.¹ More recently, another patient with IgA deficiency developed anaphylaxis with IVIG, although no anti-IgA antibodies were detected in the serum (case not published).

In a comprehensive review of the literature from the first case of anaphylaxis in a patient with IgA deficiency who received gammaglobulin, reported in 1968² to 2011, we found that anaphylaxis was reported in only 23 patients with IgA deficiency with anti-IgA antibodies after infusions with intravenous or intramuscular immunoglobulin.³ The IgA content was specified only 70% of the time; however, most reactions occurred with

products that contained $>50 \mu\text{g/mL}$ IgA, which possibly suggests a threshold phenomena. It should be noted though that

- 5 patients tolerated an IVIG product with much lower IgA content (even those with very high titers of IgG anti-IgA antibody, even up to 1:32,718 by phytohemagglutination),
- 7 patients tolerated SCIG,
- 5 patients tolerated IVIG with the same or higher IgA content (up to 2.5 mg/mL) after premedication with antihistamine and hydrocortisone, after anti-IgA titers declined, or after treatment of IVIG with autologous plasma, and
- 6 patients did not receive further IgG products.

There were a total of 49 patients with anti-IgA antibodies who tolerated gammaglobulin; 65% of these patients were on IVIG and/or SCIG. However, the specificity of anti-IgA antibodies was reported in only 18% of patients. The IgA content of the products tolerated was not specified in 63% of patients. However, several patients tolerated products with IgA content $>500 \mu\text{g/mL}$.

We concluded that

- IgG therapy should never be withheld from a patient with IgA deficiency solely because of concern for the theoretical risk of a rare serious adverse reaction.
- There are insufficient data to warrant a general recommendation for screening for anti-IgA antibodies in these patients. The predictive value of a positive result of any level is not established, although, there might be increased risk at higher levels.
- In any patient, regardless of IgA level, who is having significant systemic symptoms with IVIG, consider switching to SCIG.
- If a patient who is IgA deficient is reacting to IVIG and SCIG is not an option (eg, a high dose of IVIG is needed), then consider using a low-IgA-content product, especially if there is a high level of IgG anti-IgA antibodies.

In conclusion, in regard to your question, based on the current data in the literature, there is no evidence that choosing a product with an IgA content greater than $25 \mu\text{g/mL}$ puts the patient at a definite risk for anaphylaxis.

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